

WHAT IS CLAIMED IS:

1. A method of identifying a candidate substance that inhibits the aggregation of an aggregate-prone amyloid protein, comprising:

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- Sub B2
- (a) contacting a yeast cell that expresses an aggregate-prone amyloid protein with said candidate substance under conditions effective to allow aggregated amyloid formation; and
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- (b) determining the ability of said candidate substance to inhibit the aggregation of the aggregate-prone amyloid protein.

2. The method of claim 1, wherein the aggregate-prone amyloid protein comprises a Sup35 or URE3 polypeptide.

3. The method of claim 1, wherein the aggregate-prone amyloid protein comprises a PrP or β -amyloid polypeptide.

4. The method of claim 1, wherein the aggregate-prone amyloid protein is a chimeric protein.

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5. The method of claim 4, wherein the chimeric protein comprises at least the N-terminal domain of Sup35.

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6. The method of claim 4, wherein the chimeric protein comprises at least an aggregate forming domain of a mammalian amyloid polypeptide.

Sub B4
5 7. The method of claim 4, wherein the chimeric protein comprises at least an aggregate forming domain of an aggregate-prone amyloid protein operably attached to a detectable marker protein.

8. The method of claim 7, wherein said marker protein is green fluorescent protein or luciferase.

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9. The method of claim 7, wherein said marker protein is a drug-resistance marker protein.

10. The method of claim 7, wherein said marker protein is a hormone receptor.

11. The method of claim 10, wherein said hormone receptor is a glucocorticoid receptor.

Sub B5
12. The method of claim 6, wherein the mammalian amyloid polypeptide is PrP or β -amyloid.

25 13. The method of claim 12, wherein the chimeric protein comprises as least about amino acids 1-42 of β -amyloid protein.

Sub E4
30 14. The method of claim 4, wherein the chimeric protein comprises Sup35 in which the N-terminal domain has been replaced by amino acids 1-42 of β -amyloid protein.

15. The method of claim 1, wherein any aggregation of the aggregate-prone amyloid protein is detected by the ability of the aggregated protein to bind Congo Red.

16. The method of claim 1, wherein any aggregation of the aggregate-prone amyloid protein is detected by increased protease resistance of the aggregated protein.

17. The method of claim 1, wherein the aggregate-prone amyloid protein is labeled.

18. The method of claim 17, wherein the label is a radioactive isotope, a fluorophore, or a chromophore.

19. The method of claim 18, wherein the label is ^{35}S .

20. The method of claim 18, wherein the fluorophore comprises a green fluorescent protein polypeptide.

21. The method of claim 1, wherein any aggregation is determined by the presence of a [PSI⁺] phenotype.

22. The method of claim 1, wherein said yeast cell overexpresses Hsp104.

23. A method of identifying a candidate substance for therapeutic activity against an amyloidogenic disease in an animal, said method comprising:

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- (a) contacting a yeast cell that expresses an aggregate-prone amyloid protein with said candidate substance under conditions effective to allow amyloid formation; and
 - (b) determining the ability of said candidate substance to inhibit aggregation of the aggregate-prone amyloid protein,

10 wherein the ability to inhibit aggregation is indicative of therapeutic activity.

24. The method of claim 23, wherein the aggregate-prone amyloid protein comprises a PrP, β -amyloid, Sup35, or URE3 polypeptide.

25. The method of claim 23, wherein the protein is a chimeric protein.

26. The method of claim 25, wherein the chimeric protein comprises a Sup35 polypeptide.

27. The method of claim 25, wherein the chimeric protein comprises a mammalian amyloid polypeptide.

28. The method of claim 27, wherein the mammalian amyloid polypeptide is PrP or β -amyloid.

29. The method of claim 23, wherein any aggregation of the aggregate-prone amyloid protein is detected by the ability of the aggregation to bind Congo Red.

30. The method of claim 23, wherein the aggregate-prone amyloid protein is labeled.

31. The method of claim 30, wherein the label is a radioactive isotope, a fluorophore, or a chromophore.

32. The method of claim 31, wherein the label is ^{35}S .

33. The method of claim 31, wherein the fluorophore comprises a green fluorescent protein polypeptide.

34. The method of claim 23, wherein the aggregation of the aggregate-prone amyloid protein is determined by the presence of a [PSI⁺] phenotype.

35. The method of claim 23, wherein the disease is selected from the group consisting of Alzheimer's disease, scrapie, spongiform encephalopathy in a mammal, kuru, Creutzfeldt-Jakob disease, Gestmann-Strausser-Scheinker disease, or fatal familial insomnia.

36. The method of claim 35, wherein the mammal is bovine, feline, a mink, deer, elk, a mouse, a hamster, an ape, a monkey, or human.

Ad B7

Add D3